## Remarks/Arguments

The foregoing amendments to the claims are of formal nature, and do not add new matter. Prior to the present amendment, claims 39-51 were pending in this application and were rejected on various grounds. Claim 48 has been canceled without prejudice and claims 39-44 has been amended. The rejection to the presently pending claims are respectfully traversed.

### *Sequence Compliance*

2. Applicants have deleted the sequences on page 2, line 37 and page 14, line 17 to overcome this objection.

### *Oath/Declaration*

3. Applicants intends to file an amended Application Data sheet to fulfill the requirement of a new oath or declaration identifying this application by application number and filing date but would like to defer this compliance until allowable subject matter is indicated.

4. Applicants submit a new combined oath/declaration executed by Wei-Qiang Gao to overcome the Examiner's objection.

### *Specification*

5. The specification has been objected to for containing an embedded hyperlink. The foregoing amendment, which deleted all embedded hyperlinks or other forms of browser executable code, is believed to overcome this objection.

6. Applicants submit that Table 1 is a computer program while Tables 2-6 comply with 37 C.F.R. 1.55(c) format.

### *Claim Rejections – 35 USC § 101*

7. Claims 39-51 were rejected under 35 U.S.C. §101 allegedly "because the claimed invention is drawn to an invention with no apparent or disclosed specific and substantial credible utility." The Examiner specifically noted that "the instant specification does not disclose the biological role of this protein or its significance." The rejection is respectfully traversed.

*Utility – Legal Standard*

According to the Utility Examination Guidelines ("Utility Guidelines"), 66 Fed. Reg. 1092 (2001) an invention complies with the utility requirement of 35 U.S.C. § 101, if it has at least one asserted "specific, substantial, and credible utility" or a "well-established utility."

Under the Utility Guidelines, a utility is "specific" when it is particular to the subject matter claimed. For example, it is generally not enough to state that a nucleic acid is useful as a diagnostic without also identifying the conditions that is to be diagnosed.

The requirement of "substantial utility" defines a "real world" use, and derives from the Supreme Court's holding in *Brenner v. Manson*, 383 U.S. 519, 534 (1966) stating that "The basic *quid pro quo* contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility." In explaining the "substantial utility" standard, M.P.E.P. 2107.01 cautions, however, that Office personnel must be careful not to interpret the phrase "immediate benefit to the public" or similar formulations used in certain court decisions to mean that products or services based on the claimed invention must be "currently available" to the public in order to satisfy the utility requirement. "Rather, **any reasonable use that an applicant has identified for the invention that can be viewed as providing a public benefit should be accepted as sufficient**, at least with regard to defining a "substantial" utility." (M.P.E.P. 2107.01, emphasis added.) Indeed, the Guidelines for Examination of Applications for Compliance With the Utility Requirement, set forth in M.P.E.P, 2107 II (B) (1) gives the following instruction to patent examiners: "If the applicant has asserted that the claimed invention is useful for any particular practical purpose . . . and the assertion would be considered credible by a person of ordinary skill in the art, do not impose a rejection based on lack of utility."

Finally, the Utility Guidelines restate the Patent Office's long established position that any asserted utility has to be "credible." "Credibility is assessed from the perspective of one of ordinary skill in the art in view of the disclosure and any other evidence of record . . . that is probative of the applicant's assertions." (M.P.E.P. 2107 II (B) (1) (ii)) Such standard is presumptively satisfied unless the logic underlying the assertion is seriously flawed, or if the facts upon which the assertion is based are inconsistent with the logic underlying the assertion (Revised Interim Utility Guidelines Training Materials, 1999).

*Proper Application of the Legal Standard*

Applicants submit that the invention defined by the presently amended claims has a specific, substantial and credible asserted utility, and is sufficiently described in the specification. Applicants rely on the gene amplification data (Example 92) for support of patentable utility for the PRO187 polypeptide. This data was first disclosed in International Application No. PCT/US98/18824, filed on September 10, 1998, the priority of which is claimed in the present application. Hence, the effective filing date of the present application is September 10, 1998.

Gene amplification is an essential mechanism for oncogene activation. It is well known that gene amplification occurs in most solid tumors, and generally is associated with poor prognosis. As described in Example 92 of the present application, the inventors isolated genomic DNA from a variety of primary cancers and cancer cell lines that are listed in Table 9 (pages 229-234 of the specification), including primary lung and colon cancers of the type and stage indicated in Table 8 (page 227). As a negative control, DNA was isolated from the cells of ten normal healthy individuals, which was pooled and used as a control (page 222, lines 34-36). Gene amplification was monitored using real-time quantitative TaqMan™ PCR. The gene amplification results are set forth in Table 9. As explained in the passage bridging pages 222 and 223, the results of TaqMan™ PCR are reported in ΔCt units. One unit corresponds to one PCR cycle or approximately a 2-fold amplification, relative to control, two units correspond to 4-fold, 3 units to 8-fold, etc. amplification. PRO187 showed approximately 1.67-4.05 fold amplification in 6 primary lung tumors and upto 3.56 fold amplification in 10 primary colon tumors, which are way above figures considered significant. Hence, these data clearly support a role of PRO187 as a lung and colon tumor marker.

The attached Declaration by Audrey Goddard clearly establishes that the TaqMan™ real-time PCR method described in Example 92 has gained wide recognition for its versatility, sensitivity and accuracy, and is in extensive use for the study of gene amplification. The Declaration also confirms that based upon the gene amplification results set forth in Table 9 one of ordinary skill would find it credible that PRO187 is a diagnostic marker of human lung and colon cancer. It is, of course, true that further research might be needed to develop PRO187 into a diagnostic product. However, the fact that such follow-up tests might be necessary, cannot properly lead to the legal conclusion that PRO187 lacks patentable utility.

As set forth in M.P.E.P, 2107 II (B) (1), if the applicant has asserted that the claimed invention is useful for any particular practical purpose, and the assertion would be considered credible by a person of ordinary skill in the art, a rejection based on lack of utility should not be imposed. The attached Declaration by Audrey Goddard establishes that the asserted utility in viewed "credible" by one skilled in the art. Indeed, the logic underlying Applicants' assertion that PRO187 is a diagnostic marker of lung cancer cannot be viewed as "seriously flawed," and the facts upon which the assertion is based are not inconsistent with the logic underlying the assertion. It is always possible that an invention fails on its way of development to a commercial product. Thus, despite recent advances in rational drug design, a large percentage of drug candidates fails, and never makes it into a drug product. However, the USPTO is not the FDA, the law does not require that a product (drug or diagnostic) be currently available to the public in order to satisfy the utility requirement.

Accordingly, the Examiner is respectfully requested to reconsider and withdraw the present rejection.

*Claim Rejections – 35 USC § 112/Enablement*

Claims 39-51 have been rejected under 35 USC §112, first paragraph because "the claimed invention is not supported by either a clear asserted or well- established utility." The Examiner also noted that "the specification only describes a polypeptide having the amino acid sequence of SEQ ID NO:23 and fails to teach or describe any other polypeptide which lacks the amino acid sequence of SEQ ID NO:23 and has the activities possessed by the isolated polypeptide. Therefore, there is a lack of guidance or teaching regarding structure and function because there is only a single example provided in the specification and because there is no guidance found in the prior art." Further, the Examiner notes that the deposited plasmid and/or microorganism does not appear to be enabled for lack of public availability.

In response to the previous rejection under 35 U.S.C. 101, Applicants have shown that the specification discloses a substantial, specific and credible utility in the gene amplification data for the PRO187 polypeptides. This specific utility is now recited in the rejected claims by the recitation that the claimed polypeptides are "associated with formation of lung and colon tumors." It is submitted that one skilled in the art, was able to practice the claimed invention at the effective priority date of this application, without undue experimentation. Accordingly, the

Examiner is respectfully requested to reconsider and withdraw the rejection of all pending claims under this section.

Also, the amendments to the specification have incorporated the requisite assurances "that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of the pertinent U.S. patent." Thus, the Examiner is respectfully requested to reconsider and withdraw the present rejection.

*35 USC § 112, First Paragraph/Written Description*

Claims 39-43 have been rejected for alleged lack of sufficient written description within the full scope of claims. The Examiner noted that "the claims are drawn to isolated polypeptides having 80%, 85%, 95%, 90%, 95% or 99% sequence identity to SEQ ID NO:23/ ATCC Deposit #209375." In particular, the Examiner acknowledged that "From the specification, it is clear that Applicant has possession of a nucleic acid which encodes a protein with amino acid of SEQ ID NO:23/ ATCC Deposit #209375." The Examiner further notes that the claims are not directed to only polypeptides encoded by SEQ ID NO: 23 while the specification does not described any other polypeptide which lacks amino acid of SEQ ID NO: 23.

Applicants submit that the amended claims now recite polypeptides associated with formation of lung and colon tumors which further defines the properties of the polypeptides. Accordingly, it is no longer true that the claims are drawn to a genus of polypeptides defined by sequence identity alone. Coupled with the general knowledge available in the art at the time of the invention, the specification provides ample written support for such polypeptides in Example 92 where gene amplification results are described. Thus, one skilled in the art would have known at the time of the invention, that the Applicants had possession of the claimed polypetides.

The Examiner is therefore respectfully requested to reconsider and withdraw the present rejection.

*35 USC § 112, Second Paragraph*

Claims 39-51 were rejected under 35 U.S.C. §112, second paragraph, allegedly, as being indefinite for reciting "the polypeptide...lacking its associated signal peptide" and "the

extracellular domain...lacking its associated signal sequence", that is, parts (b) and (d) of the claim. Claims 45 and 49-52 are indefinite for depending on indefinite claims.

The foregoing amendments wherein such references have been deleted in the claims are believed to overcome this rejection. Thus, dependent claims 45 and 49-52 are also definite.

Hence, Applicants respectfully request withdrawal of the current rejection.

The present application is believed to be in *prima facie* condition for allowance, and an early action to that effect is respectfully solicited.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 08-1641 (Attorney Docket No.: 39780-1618P2C1). Please direct any calls in connection with this application to the undersigned at the number provided below.

Respectfully submitted,

Date: June 6, 2003

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